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EXAMINER: KISHORE, G
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DATE MAILED: 07/06/00

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-44 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-44 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

DETAILED ACTION

Claims included in the prosecution are 1-44.

Claim Rejections - 35 U.S.C. § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

2. Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for drop in blood pressure as the adverse reactions and indomethacin as the drug which can treat this pressure drop, does not reasonably provide enablement for generic 'adverse reactions' and 'antiinflammatory agent'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. .

Instant invention is based on the observation that liposomes made with specific phospholipids cause a drop in blood pressure and that indomethacin is able to correct this blood pressure drop. Indomethacin might come under the classification of 'antiinflammatory drugs' because it has antiinflammatory properties; just because indomethacin also possesses blood pressure modulating properties, one cannot conclude that all anti-inflammatory agents which is a generic name and includes a variety of compounds are also blood pressure modulating agents. Applicants have provided no

rationale for this concept. Secondly and most importantly, liposomes are known in the art as drug delivery agents for the past 20 years and as the prior art would indicate that even the administration of empty liposomes is known. Applicants have not shown that or provided adequate description as to what other adverse reactions are caused by the liposomes and presented a rationale for the capability of indomethacin to correct all the adverse reactions. Broad claims must have broad basis of support in the specification; in the absence of such support, claims must be limited to liposomes made with specific phospholipids and the drop in blood pressure as the adverse reaction and indomethacin as the compound which is able to correct this adverse reaction.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> **The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.**

4. Claims 18-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

What is being conveyed through claim 18? What is the animal treated for? What is the distinction between the 'bioactive agent' and 'anti-inflammatory agent'? If the liposome composition induces adverse reaction, it is unclear why it is administered and how this adverse reaction is reduced. Also unclear as to how the treatment with an

antiinflammatory agent reduces all the adverse reactions. Antiinflammatory agent is supposed to reduce only inflammation. This claim requires restructuring. Similar is the case with the independent claims 23 and 24 and other independent claims..

The term 'surface modified agent' in claims 36-38 and the term, 'the anchor' in claim 41 have no antecedent basis in claim 25.

Claim Rejections - 35 U.S.C. § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless --**
>
> **(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

6. Claims 18, 21, 23, 25 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Mezei (Life Sciences, 1980).

Mezei teaches liposomes containing a steroid (antiinflammatory agent) and a method of treating an animal. The liposomes are multilamellar and hence have instant sizes (note the abstract and entire article).

7. Claims 18, 20, 22, 25, 26 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by JP 60152414 or JP 63264517.

Both JP references disclose liposomes containing indomethacin (note the abstracts) and a method of treatment.

8. Claims 18, 19, 21, 23, 24, 25, 27, 33-36, and 43-44 are rejected under 35 U.S.C. 102(b) as being anticipated by Young (5,023,087).

Young discloses a method of treating an animal with liposomes containing an antiinflammatory agent (steroids) and empty liposomes; the liposomes are either unilamellar or multilamellar (note the abstract, col. 4, line 62 et seq., col. 10, line 35 et seq., examples).

Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.**

10. Claims 33-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 63264517 or Young cited above individually or in combination, further in view of Park (BBA, 1992): or Park in view of either of Young or JP.

What is lacking in JP and Young is the teaching the modification of the surface of the liposomes using carboxylic acids.

Park teaches that liposomes modified with carboxylic acids prolong the circulation of the liposomes (note the abstract). Park's teachings are generic with respect to the active agent incorporated.

The modification of the surface of the liposomes of JP or Young using carboxylic acids would have been obvious to one of ordinary skill in the art since such a modification results in the liposomes having longer circulation. Alternately, to encapsulate an antiinflammatory agent as the active agent in the liposomes of Park would have been obvious to one of ordinary skill in the art since liposomes are known drug delivery agents and the references of JP and Young show the knowledge in the art of encapsulation of antiinflammatory agents in liposomes for delivery.

11. Claims 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 63264517 or Young cited above by themselves, in further in view of Park (BBA, 1992): or Park in view of either of Young or JP as set forth above, and in further combination with Cheng (Investigative Radiology, vol. 22, 1987) .

The references of JP, Young and Park do not teach the inclusion of a contrast agent in the liposomes. Such an inclusion however, would have been obvious to one of ordinary skill in the art if the purpose is to locate the treatment site as well as treat it since the reference of Cheng shows the awareness in the art of encapsulating contrast agents in liposomes (note the abstract).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to *G.S. Kishore* whose telephone number is (703) 308-2440.

The examiner can normally be reached on Monday-Thursday from 6:30 A.M. to 4:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, T.K. Page, can be reached on (703)308-2927. The fax phone number for this Group is (703)305-3592.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [thurman.page@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703)308-1235.

Gollamudi S. Kishore, Ph. D

Primary Examiner

Group 1600

gsk

June 29, 2000